

What is claimed is:

1. A method for modulating viral RNA replication and translation, in a eukaryotic cell, of positive-strand viral RNA, comprising the step of contacting a viral RNA-binding protein (vRbp) with a compound that modulates an activity of said vRbp.
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2. The method of claim 1, wherein said vRbp is selected from the group consisting of: vRbp130, vRbp120, vRbp110, vRbp84, vRbp64, and vRbp45.
- 10 3. The method of claim 1 wherein said activity of the vRbp is selected from the group consisting of:
 - a response to viral RNA,
 - a response to interferon induction,
 - a response to double-stranded RNA-dependent protein kinase (PKR), and
 - 15 a response to vRbp.
4. The method of claim 3 wherein said response is formation of a viral:cellular ribonucleoprotein (RNP) complex.
- 20 5. The method of claim 4 wherein said RNP complex comprises a viral RNA:vRbp interaction.
6. The method of claim 5 wherein said viral RNA:vRbp interaction comprises binding of a vRbp to a viral RNA 3' untranslated region (3'UTR).
- 25 7. The method of claim 4 wherein said viral RNA:vRbp interaction comprises binding of a vRbp to a viral RNA 5' untranslated region (5'UTR).
8. The method of claim 5 wherein said 3'UTR is a UGA box consensus sequence.
- 30 9. The method of claim 3 wherein said response is viral circularization.
10. The method of claim 9 wherein said viral circularization comprises binding of vRbp to the viral 5'UTR and 3'UTR creating a physical and functional link between both ends of the RNA.
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11. The method of claim 9 wherein said viral circularization comprises an interaction between viral 5'UTR, 3'UTR RNA, vRbp, and cellular proteins involved in the interferon antiviral response.
- 5 12. The method of claim 3 wherein said response is increase in translational frameshifting that result in decreased viral replication.
13. The method of claim 3 wherein said response is formation of a vRbp:PKR interaction.
- 10 14. The method of claim 1 wherein said viral replication and translation comprises coordinated regulation of replication and translation of viral RNA.
15. The method of claim 1, wherein said eukaryotic cell is a mammalian cell.
- 15 16. The method of claim 1, wherein said eukaryotic cell is a human cell.
17. The method of claim 1, wherein said eukaryotic cell is a liver cell.
18. The method of claim 1, wherein said positive strand viral RNA comprises RNA from a
20 member of the family *Flaviviridae*.
19. The method of claim 1 wherein said positive strand viral RNA comprises RNA from a member of the family *Picornaviridae*.
- 25 20. The method of claim 1 wherein said compound comprises therapeutically effective amounts of viral 3'UTR, fragments thereof, or pharmaceutically acceptable derivatives thereof.
21. The method of claim 1 wherein vRbp activity is reduced by interfering with the interaction between vRbp and vRbp recognition sites on viral RNA.
- 30 22. The method of claim 1 wherein vRbp activity is reduced by modification of a viral 3'UTR, which modification otherwise reduces vRbp binding to vRbp recognition sites on viral RNA.

23. The method of claim 1 wherein vRbp activity is reduced by inhibiting dissociation of viral RNA:vRbp complexes.
24. A method for reducing the effects of viral infection on eukaryotic cells, comprising
5 inhibiting vRbp activity in the cell such that viral replication and translation of viral RNA is regulated by interactions between vRbp and said viral RNA, comprising introducing a nucleic acid decoy molecule into the cell in an amount sufficient to inhibit viral RNA:vRbp interactions, which decoy includes a vRbp recognition site that binds to vRbp.
- 10 25. A method for reducing the effects of viral infection on eukaryotic cells, comprising inhibiting vRbp activity in the cell such that viral replication and translation of viral RNA is regulated by interactions between vRbp and PKR, comprising introducing a nucleic acid decoy molecule into the cell in an amount sufficient to inhibit vRbp:PKR interactions,
15 which decoy includes a vRbp recognition site that binds to vRbp.
26. A method for reducing the effects of viral infection on eukaryotic cells, comprising the step of reducing vRbp activity in the cell such that viral replication and translation is reduced.
27. A method for reducing the effects of viral infection on eukaryotic cells, the method
20 comprising the step of reducing vRbp activity in the cell such that production of novel infectious virus particles is reduced.
28. A method for reducing the effects of viral infection on eukaryotic cells, the method
25 comprising the steps of reducing vRbp activity in the cell to inhibit the spread of virus in infected individuals and animals.
29. A method for reducing the effects of viral infection on eukaryotic cells, the method
30 comprising the steps of reducing vRbp activity in the cell to prevent the spread of virus between different individuals and animals.
30. A method for reducing the effects of viral infection on eukaryotic cells, the method comprising the steps of reducing vRbp activity in the cell to treat syndromes caused by co-infection of different viruses.

31. The method of claim 30 wherein different viruses comprise HCV and HBV or HCV and HIV.
32. A method for reducing the effects of viral infection on eukaryotic cells, the method
5 comprising the steps of reducing vRbp activity in the cell to treat before, during, and after a transplantation.
33. A method for reducing the effects of viral infection on eukaryotic cells, the method
10 comprising the steps of modulating vRbp activity in the cell to treat immunosuppressed patients to prevent virus infections.
34. A method for reducing the effects of viral infection, in a eukaryotic cell, by modulating
15 vRbp activity in the cell, the method comprising the step of interfering with viral translation termination as a mechanism to disrupt viral replication.
35. A method for reducing the effects of viral infection, in a eukaryotic cell, by modulating
20 viral RNA-binding protein (vRbp) activity in the cell, the method comprising the step of interfering with interactions between viral 3'UTR and 5'UTR, or interactions between structural elements within the 3'UTR and NS5B stop codon as a mechanism to regulate translation termination, translational frameshifting, and the coordinated balance of replication and translation on positive strand RNA.
36. A method of treating or preventing a viral infection by a virus comprising the step of
25 administering a therapeutically effective amount of a compound to an individual suspected of having or being at risk of having an infection with a virus.
37. The method of claim 35 wherein said positive strand viral RNA comprises RNA from a member of the family *Flaviviridae*.
- 30 38. The method of claim 35 wherein said positive strand viral RNA comprises RNA from a member of the family *Picornaviridae*.
39. The method of claim 36 wherein said virus is selected from the group consisting of: hepatitis
35 A virus (HAV), hepatitis C virus (HCV), human Rhinovirus (HRV), bovine viral diarrhea virus (BVDV), and classical swine fever virus (CSFV).

40. The method of claim 36 wherein said compound interacts with viral genomic 3'UTR or 5'UTR RNA.

5 41. A method for modulating the function of a viral 3'UTR comprising the step of contacting a 3'UTR with a compound that modulates the structure of the 3'UTR as to inhibit the interaction between 3'UTR and vRbp.

10 42. A method for screening to identify compounds that activate or that inhibit the function of vRbp which comprises a method selected from the group consisting of:

(a) mixing a candidate compound with a solution containing a vRbp, to form a mixture, measuring activity of the vRbp in the mixture, and comparing the activity of the mixture to a standard;

15 (b) detecting the effect of a candidate compound on the production of viral RNA in a eukaryotic cell, using for instance, an ELISA assay, reticulocyte lysate translation assay (luciferase RNA); and

(c) (1) contacting a composition comprising the vRbp with the compound to be screened under conditions to permit interaction between the compound and the vRbp to assess the interaction of a compound, such interaction being associated with a second component capable of providing a detectable signal in response to the interaction of the vRbp with the compound; and

20 (2) determining whether the compound interacts with and activates or inhibits an activity of the vRbp by detecting the presence or absence of a signal generated from the interaction of the compound with the vRbp.

25 43. A method for screening to identify compounds that increase translational frameshifting resulting in decreased replication of viral RNA comprising a method selected from the group consisting of:

30 (a) mixing a candidate compound with a solution containing a vRbp, to form a mixture, measuring activity of the vRbp in the mixture, and comparing the activity of the mixture to a standard; and

(b) detecting the effect of a candidate compound on the production of viral RNA in a eukaryotic cell, using for instance, an ELISA assay, reticulocyte lysate translation assay (luciferase RNA).

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44. The method of claim 43 wherein said viral RNA is positive strand viral RNA.

45. The method of claim 44 wherein said positive strand viral RNA comprises RNA from a member of the family *Flaviviridae*.

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46. The method of claim 44 wherein said positive strand viral RNA comprises RNA from a member of the family *Picornaviridae*.